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Case Report

A fatal case of pontine hemorrhage related to methamphetamine abuse

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Abstract

In this report, we describe a fatal case of pontine hemorrhage related with methamphetamine abuse. A 54-year-old male was found dead in a prone position in his parents' house, and a medico-legal autopsy was carried out to determine the cause of his death. Externally, although an injection mark-like injury with subcutaneous hemorrhage was observed in the left cubital fossa, the autopsy revealed no severe trauma leading to death. Internally, every organ was moderately congested. The brain weighed 1330 g. Macroscopically, there was no vascular abnormality such as aneurysm or malformation. In the sections of the brain stem, a massive hematoma occupied the central area of the pons. Drug screening test using Triage™ was weakly positive for amphetamines. Moreover, in the blood and urine samples, methamphetamine was quantitatively detected at concentrations of 0.4 and 0.6 mg/l, respectively, by gas chromatography–mass spectrometry. Other drugs and poison were not detected in the blood and urine samples collected at autopsy. Histopathologically, necrotizing angiitis characterized by fibrinoid necrosis of the intima and media was observed with cell infiltration. Thus, the pontine hemorrhage seemingly resulted from methamphetamine-induced angiitis, with an acute elevation of blood pressure after methamphetamine abuse.

Keywords: Forensic pathology; Drug abuse; Methamaphetamine; Intracerebral hemorrhage; Necrotizing angiitis

1. Introduction

Drug abuse has become a serious social problem worldwide. In Japan, the Stimulant Control Law prohibits unauthorized possession, use or distribution of methamphetamine and amphetamine. In particular, methamphetamine abuse has continued to increase in Japan. Methamphetamine may be snorted, injected intravenously, taken orally, or smoked, resulting in intense euphoria and addictive potential. The sympathomimetic effects of methamphetamine include an elevation of pulse rate and blood pressure, increased alertness, decreased fatigue, and suppression of appetite.[1,2] Methamphetamine abuse causes hyperthermia, arrhythmia and fugitive hypertension, occasionally resulting in a fatal outcome.[1,2] In particular, several previous reports stated that methamphetamine abuse increased the risk of cerebral vascular accidents such as hemorrhagic or ischemic stroke, and subarachnoid hemorrhage even in young persons aged less than 20 years.[3–7] In this report, we describe a fatal case of pontine hemorrhage, presumably due to intravenous self-administration of methamphetamine.

2. Case profile

A 54-year-old male visited his parents' house at 11:00 PM. At that time, he was nauseous with mild numbness of the extremities, but went to sleep without any medication. Next day, at 4:25 PM, his mother tried to wake him but he did not reply, and she found his body in a prone position. According to the police investigation, no criminal

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activity was identified. Thus, a forensic autopsy was performed to clarify the cause of his death at our department.

3. Autopsy findings

The deceased was 162 cm tall and weighed 51 kg. Postmortem rigidity remained slightly in the joints of the jaw, neck and fingers, and moderately in the other joints. Livor mortis, dark red in color, was found on the back and the upper part of the chest. When pressed, it did not disappear. Dark green putrefactive discoloration was slightly observed on the abdomen. Although the face was moderately congested, there were no apparent petechial hemorrhages in the palpebral conjunctivae. The diameter of both pupils was 6 mm. An injection mark-like injury with subcutaneous hemorrhage was observed in the left cubital fossa. However, there were no severe injuries leading to death. Internally, there was 10 ml of light red fluid in the pericardiac cavity, and intracardiac blood with no soft hemocoagula was dark-red in color (250 ml). The heart weighed 390 g, showing moderate cardiomegaly, and myocardial fibrosis could be faintly observed at the anterior wall of the left ventricle. However, there were no pathological changes leading him to the death. The left and right lungs were edematous and weighed 550 and 580 g, respectively. The brain, weighing 1330 g, was remarkably edematous. In sections of the brain, the center of the pons was almost filled with hematoma (Fig. 1). The stomach contained 40 ml of reddish brown viscous fluid. The bladder contained 280 ml of slightly yellowish urine. The other organs showed no remarkable pathological findings.

Histopathologically, necrotizing angiitis, characterized by fibrinoid necrosis of the intima and media with cell infiltration, was observed in many arteries of the pons and cerebrum. Necrotic lesions showed the absence of nuclei, atrophy with increased eosinophilic smooth muscle, and decreased medial thickness (Fig. 2). In consistent with macroscopic view of the heart, cardiomyocytes seemed to be slightly hypertrophic. Moreover, fibrotic changes could be confirmed on the anterior wall of the left ventricle, and moderate stenosis was also recognized in the left anterior descending coronary artery. However, no histopathological changes indicating fresh myocardial infarction could be detected.

Fig. 1. Macroscopic view of the pontine hemorrhages. In sections of the pons, the central portion is almost totally occupied by massive hematoma.

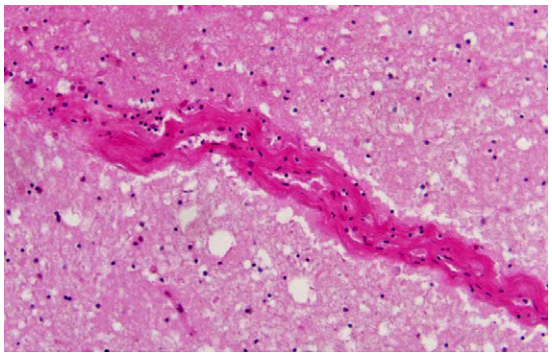

Fig. 2. Histopathological view of the pons. Necrotizing angiitis characterized by fibrinoid necrosis of the intima and media is observed with cell infiltration.

A drug screening test using Triage™ (BIOSITE, San Diego, CA) was weakly positive for amphetamines. Moreover, in the blood and urine samples, methamphetamine was detected at concentrations of 0.4 and 0.6 mg/l, respectively, by gas chromatography–mass spectrometry. Other drugs and poisons were not detected in both samples.

4. Discussion

Etiologically, about half of all intracerebral hemorrhages seem to be caused by hypertension.[8] The remaining non-hypertensive intracerebral hemorrhages are caused by cerebral amyloid angiopathy, anticoagulants, tumors, drugs, thrombocytopenia, and hemophilia. Hemorrhagic strokes most frequently occur in the putamen and thalamus, followed by the cerebellum.[8] The frequency of pontine hemorrhage is the lowest. In the present case, the deceased had no past history of hypertension. However, methamphetamine was detected at a concentration of 0.4 mg/l in the blood sample, which was considered toxic but not lethal level.[9] Thus, we have to discuss the relationship between pontine hemorrhage and methamphetamine.

Several lines of accumulating evidence have demonstrated that methamphetamine abuse is an important risk factor for cerebral vascular accidents (CVA) such as cerebral infarction or intracerebral hemorrhage, even without an apparent past history of hypertension.[3–7,10–34] In general, hemorrhagic strokes account for less than one fourth of all cerebral vascular accidents. However, methamphetamine-related CVA predominantly induces hemorrhagic

strokes. Hemorrhages are most often confined to the frontal lobes, although they occasionally involve the basal ganglia. This distribution is in contrast with the pattern of hypertensive hemorrhages. To the best of our knowledge, since the first case of methamphetamine-related intracerebral hemorrhage was reported in 1945, 36 methamphetamine-related intracranial hemorrhage cases confirmed by angiography, computed tomography or autopsy have been reported, consisting of 20 survival and 16 fatal cases.[3–7,10–34] In comparison with hypertensive CVA, methamphetamine-related CVA apparently occurs in younger persons. Generally, vascular abnormalities such as congenital aneurysm or arterio-venous malformation often account for CVA in younger persons. However, there were only 4 cases of vascular abnormalities among the 36 cases. Methamphetamine-related hemorrhagic strokes are more often intracerebral or simultaneously intracerebral and subarachnoid than only subarachnoid. Actually, among them, 20 and 6 cases showed intracerebral hemorrhage and subarachnoid hemorrhage, respectively. Both were observed in 8 cases. Only two cases were presumed to be pure intraventricular hemorrhage without expansion to cerebral parenchymal hemorrhages.

Although the mechanism of amphetamine-related intracranial hemorrhages remains elusive, several mechanisms have been proposed. Because of the sympathomimetic effects of methamphetamine by the release of norepinephrine, significant elevation of blood pressure and cerebral arterial spasm are induced, eventually resulting in cerebral vascular accident.[1,2] Moreover, cerebral vasculitis was most commonly described in methamphetamine abusers with either hemorrhagic or ischemic strokes. Radiologically, cerebral vasculitis associated with methamphetamine is described on the arteriography of cerebral vessels, which shows diffusely pronounced irregularity of flow with arterial narrowing and beading.[4,10,12,19,21,35,36] Although methamphetamine-related angiitis was reversible, it could be rapidly caused by only a single use of methamphetamine.[35,36] These observations imply that methamphetamine has direct toxic effects on the cerebral vasculature. Citron et al.[37] reported 14 cases of necrotizing angiitis associated with drug abuse such as narcotics, hallucinogens, stimulants, and sedatives. In particular, methamphetamine was the most common. Histopathologically, this alteration can be characterized by fibrinoid degeneration of the intima and media, with cellular infiltration. Moreover, Chen et al.[38] reported a rare case of a rapidly growing aneurysm in the major intracranial vessels resulting from methamphetamine abuse. Although, in Karch's autopsy series of 413 methamphetamine users, there were a total of 10 intracerebral hemorrhage cases, pontine hemorrhage was never found. Moreover, the 10 cases were not associated with necrotizing angiitis, indicating that they were possibly caused by sympathomimetic effects of methamphetamine.[39] Our histopathological findings of the arteries of the pons and cerebrum were consistent with the characteristics of necrotizing angiitis described previously. Thus, the vasculitis resulting from methamphetamine abuse possibly caused pontine hemorrhage in the present case, indicating relatively rare case.

According to the comprehensive study by Karch and his colleagues, methamphetamine abusers often showed the abnormality in the cardiovascular system, compared with the controls. Briefly, cardiac enlargement, coronary artery disease ranging from the minimal to severe multivessels, and myocardial fibrosis were detected with a high incidence, implying that long-term use of methamphetamine.[39] Consistently, in the present case, cardiovascular abnormalities mentioned above could be observed macro- and microscopically. Moreover, cardiomyopathy was also well known as a complication of methamphetamine abuse.[40–42] Catecholamine excess due to methamphetamine use, seemingly accounts for these cardiovascular abnormalities.[1]

In the present case, the blood methamphetamine concentration was 0.4 mg/l, indicating a toxic but not lethal level.[9] There are two independent studies using a similar protocol about the blood concentration of methamphetamine in its user's deaths.[39,43] In methamphetamine-related deaths, in which methamphetamine was demonstrated in the blood but did not directly cause death, the blood methamphetamine concentrations were 0.05–9.30 mg/l (median: 0.42 mg/l, $n = 92$) in Logan's series, and 1.78 ± 0.27 mg/l (mean $\pm$ SE, $n = 141$) in Karch's series, respectively.[39,43] These results suggested that the blood methamphetamine concentrations were variable in methamphetamine-related deaths. Moreover, in their series, the extensive overlap in the value was found between death cases due to direct toxic effects of methamphetamine and methamphetamine-related death cases.[39,43] Thus, as pointed out by Logan et al. [43] blood methamphetamine concentration should not be interpreted in isolation, and it is important to perform autopsy in order to understand and properly certify deaths.

Finally, when intracerebral hemorrhage is encountered in forensic practice, the abuse of drugs such as methamphetamine, cocaine, and so on should always be taken into consideration as its cause.

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